

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gary L. Nelsestuen  
Title : MODIFIED VITAMIN K-DEPENDENT POLYPEPTIDES

Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Specification

Please replace the paragraph beginning at page 1, line 4 with the following rewritten paragraph:

--This application is a continuation of U.S. Serial No. 09/302,239, filed April 29, 1999, which is a continuation-in-part of U.S. Serial No. 08/955,636, filed on October 23, 1997, now issued as U.S. Patent No. 6,017,882.--

In the Claims

Please cancel claims 1-22.

Please add the following new claims.

--23. A protein C or activated protein C polypeptide comprising a modified GLA domain, said modified GLA domain comprising at least one amino acid substitution selected from residues 11, 12, 29, 33 and 34.

CERTIFICATE OF MAILING BY EXPRESS MAIL

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Date of Deposit

[Signature]  
Signature

Vince Defante  
Typed or Printed Name of Person Signing Certificate

24. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 11.
25. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 12.
26. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 29.
27. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 33.
28. The protein C or activated protein C polypeptide of claim 23, wherein said at least one amino acid substitution is at residue 34.
29. A protein C or activated protein C polypeptide comprising a modified GLA domain, said modified GLA domain comprising three amino acid substitutions at positions selected from the group consisting of residues 11, 12, 29, 33 and 34.
30. The protein C or activated protein C polypeptide of claim 29, wherein said three amino acid substitutions are at residues 12, 33 and 34.
31. The protein C or activated protein C polypeptide of claim 30, wherein residue 33 is glutamic acid.
32. The protein C or activated protein C polypeptide of claim 30, wherein residue 34 is aspartic acid.
33. The protein C or activated protein C polypeptide of claim 30, wherein residue 33 is glutamic acid and residue 34 is aspartic acid.

34. The protein C or activated protein C polypeptide of claim 29, wherein residue 11 is glutamine.
35. A pharmaceutical composition comprising said protein C or activated protein C polypeptide of any one of claims 23-34 and a pharmaceutically acceptable carrier.
36. The composition of claim 35 for use in treating thrombosis in a mammal.
37. The composition of claim 35 for use in decreasing clot formation in a mammal.
38. The composition of claim 36, wherein said composition is formulated for parenteral administration to a human patient.
39. The composition of claim 37, wherein said composition is formulated for parenteral administration to a human patient.
40. An isolated nucleic acid, said nucleic acid comprising a nucleic acid sequence encoding said protein C or activated protein C polypeptide of claim 23 or claim 29.
41. A method of producing the protein C or activated protein C polypeptide of any one of claims 23-34, said method comprising expressing an isolated nucleic acid encoding said protein C or activated protein C polypeptide in a mammalian host cell.
42. The method of claim 40, wherein said mammalian host cell is an adenovirus-transfected human kidney 293 cell.--

REMARKS

Applicants have canceled claims 1-22 and submitted new claims 23-41. Support for these claims can be found throughout the specification, including at page 9, lines 14-20, page 10, line 10 through page 11, line 14, page 13, lines 26-27, page 15, lines 22-25, page 17, lines 18-20, and at page 33, lines 25-28. No new matter has been introduced.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Applicant submits that all of the claims are now in condition for examination, which action is requested.

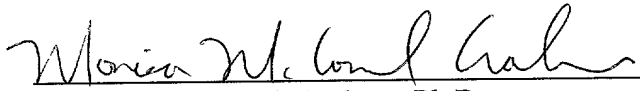
A check is enclosed for payment of excess claim fees.

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: \_\_\_\_\_

3/12/01

  
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**Version with markings to show changes made**

In the specification:

Paragraph beginning at page 1, line 4 has been amended as follows:

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